

## **REMARKS**

### **(a) Restriction/Election Requirement**

On June 9, 2003, the Examiner issued a telephonic 6-way restriction of the claims of the subject application. In a reply faxed on June 16, 2003, the undersigned, as Applicants' legal representative, elected, without traverse, the invention of Group I. Group I is defined by claims 1, 2 (in part), 6-9 and 14 (in part), and is drawn to the compounds of formula II (*i.e.* the combination of formula I with formula Ia). Non-elected claims 3-5, 10-13 and 15 have been canceled without prejudice and with the understanding that Applicants may choose to pursue them in a divisional application. Method claim 16 has been amended to be commensurate with the scope of claim 1. The Examiner may withdraw this claim as unelected but it will be rejoined upon allowance of the composition claims.

### **(b) Amendments to the Specification**

The amendments to pages 23 and 25 of the specification, as indicated above, correct an obvious typographical error wherein  $N(R^6)$  should have been listed as  $N(R^7)$  to maintain conformity with the other  $N(R^7)$ -containing substituents of the disclosed Markush group.

The amendment to page 76 of the specification, as indicated above, corrects an obvious typographical error wherein a "7-benzyl" substituent in the product should have been described as a "7-benzyloxy" substituent. Applicants submit that it would have been clear to a person of ordinary skill in the art that the "7-benzyloxy" substituent present in the starting material of the cited Example would not have been chemically transformed under the conditions of the reaction to a "7-benzyl" substituent.

The amendment to entry No. 14 in Table VII on page 137 of the specification, as indicated above, corrects an obvious typographical error, wherein a "2-chloro-6-dimethyl" ring substitution should have been listed as a "2-chloro-6-methyl" substitution. Dimethyl substitution at the 6-position of the phenyl ring would give a disallowed pentavalent carbon atom.

No new matter has been introduced by any of the amendments.

### **(c) Amendments to the Claims**

Claims 1, 6-9 and 16 have been amended. Claims 2-5, 10-13 and 15 have been canceled without prejudice. The amendments to claims 1, 6-9 and 16 restrict these claims to the elected

subject matter of Group I. Claim 1 has been further amended to restrict the scope of Q<sup>2</sup>. No new matter has been introduced by any of the amendments. After entry of the amendments, claims 1, 6-9, 14 and 16 will be pending.

***I. REJECTION UNDER 35 U.S.C. § 112, first paragraph***

**(a) Written Description**

Claim 1 is rejected under 35 U.S.C. § 112, first paragraph, for failing to comply with the written description requirement. Specifically, the Examiner charges that the proviso in claim 1 includes a species (identified by the Examiner as being on “the last line of the claim”) which has no corresponding description in the specification.

Applicants have restricted claim 1 to the elected subject matter of the invention of Group I such that Q<sup>1</sup> is limited to the quinazoline ring of formula Ia. As amended, claim 1 does not encompass the proviso compound 1-{8-[3,4-dihydroxy-5(N-ethylcarbamoyl)tetrahydrofuran-2-yl]-7,8-dihydropteridin-4-yl}-3-(4-nitrophenyl)urea to which the Examiner takes exception. Therefore, this proviso compound, along with all other non-encompassed proviso compounds, have been deleted from claim 1, effectively mooted this ground for rejection.

**(b) Scope of Enablement**

Claims 1, 2 and 14 are rejected under 35 U.S.C. § 112, first paragraph, because the Examiner contends that the specification does not reasonably provide enablement for the preparation of the compounds of formula Ia or II where Q<sup>2</sup> is a heteroaryl, heteroaryl-(1-3C)alkyl or heteroaryl-(3-7C)cycloalkyl group.

Although Applicants disagree with the Examiner's enablement rejection, in order to expedite prosecution, claim 1 has been amended to remove the quinazoline compounds of Formula I where Q<sup>2</sup> is a heteroaryl, heteroaryl-(1-3C)alkyl or heteroaryl-(3-7C)cycloalkyl group. Claim 2 has been canceled and claim 14, being dependent from claim 1, incorporates every feature of claim 1. In light of the amendments to claim 1, Applicants request that the ground for this rejection be withdrawn.

## **II. OBJECTIONS TO THE CLAIMS**

Claims 6-9 are objected to as being dependent on a rejected base claim. The Examiner states that claims 6-9 would be allowable if rewritten in independent form, including all of the limitations of the base claim and any intervening claims.

Applicants have amended claims 6-9 such that they depend from amended claim 1, which Applicants believe is in condition for allowance. As such, Applicants request that this objection be withdrawn.

## **III. INFORMATION DISCLOSURE STATEMENT**

The following three documents are submitted in an Information Disclosure Statement that is being filed herewith:

- (a) U.S. Patent 5,773,459 (“the ‘459 patent”)
- (b) WO 98/52558 (“the WO ‘558 application”)
- (c) WO 02/00644 (“the WO ‘644 application”)

### **(a) The ‘459 Patent**

Applicants note that the ‘459 patent discloses a urea structure (see col. 2, lines 30-37) containing a R<sub>1</sub> substituent at a location that corresponds to the Q<sup>1</sup> substituent of Applicants’ claim 1. As amended, Q<sup>1</sup> has been restricted to a quinazoline ring of formula Ia. As disclosed in the ‘459 patent, R<sub>1</sub> may be a heteroaryl group. “Heterocyclic aryl” groups are defined at page 3, lines 59-65 of the ‘459 patent specification as “having from 1 to 3 heteroatoms as ring atoms in the aromatic ring and the remainder of the ring atoms are carbon atoms. Suitable heteroatoms include oxygen, sulfur and nitrogen, and include furanyl, thienyl, pyridyl, pyrrolyl, N-lower alkyl pyrrolo, pyrimidyl, pyrazinyl, imidazolyl and the like, all optionally substituted.” There is no teaching or suggestion in the ‘459 patent that a heteroaryl group may be bicyclic, and there is no disclosure of a quinazoline ring. As such, Applicants believe that the ‘459 patent can be readily distinguished from Applicants’ invention for at least this reason.

**(b) The WO '558 Application**

Applicants note that the WO '558 application discloses a urea structure of Formula I (see page 8). Either of substituents "A" or "B" of Formula I of the WO '558 application may be considered to be at a location corresponding to the Q<sup>1</sup> substituent in Formula I of Applicants' claim 1. Substituent "A" is disclosed in the WO '558 application specification at page 8, lines 12-13 as including a C<sub>5-12</sub>-heteroaryl group. Such a group may possibly encompass a quinazoline ring. However, if "A" corresponds to Applicants' Q<sup>1</sup>, then substituent "B" of the WO '558 application must correspond to Applicants' Q<sup>2</sup> substituent. As disclosed at page 8, line 14 of the WO '558 application specification, substituent "B" is restricted to thienyl, furanyl or pyrrolyl groups, *i.e.* monocyclic heteroaryl groups. As amended in Applicants' claim 1, Q<sup>2</sup> cannot be a heteroaryl group. Therefore the WO '558 application can be clearly distinguished from Applicants' invention where substituent "A" of Formula I of the WO '558 application is considered to correspond to Applicants' Q<sup>1</sup> substituent. Alternatively, substituent "B" cannot correspond to Applicants' Q<sup>1</sup> because as just discussed, "B" is restricted to monocyclic heteroaryl groups and Q<sup>1</sup> is a quinazoline ring which qualifies as a bicyclic heteroaryl group. Thus, the WO '558 application can be clearly distinguished from Applicants' invention where substituent "B" of Formula I of the WO '558 application is considered to correspond to Applicants' Q<sup>1</sup> substituent.

**(c) The WO '644 Application**

Applicants note that the WO '644 application discloses a guanidine structure of Formula I (see page 4) containing a "NR<sup>5</sup>R<sup>6</sup>" group that may be considered to correspond to the "Z" group of Formula I when "Z" is N(CN) or N(R<sup>11</sup>) as recited in Applicants' claim 1. R<sup>11</sup> is restricted to a hydrogen or a (1-6C)alkyl group. The WO '644 application can be readily distinguished from Applicants' claimed invention for at least the reason that the R<sup>6</sup> substituent of the NR<sup>5</sup>R<sup>6</sup> group is limited to substituents other than CN, hydrogen or a (1-6C)alkyl group.

**IV. CONCLUSION**

All remaining grounds for rejection have been addressed and overcome by the above amendments and remarks. It is therefore believed that all claims presently pending in this

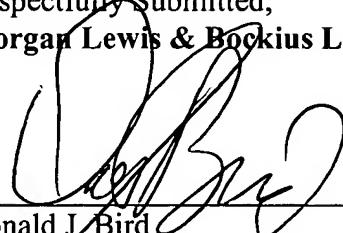
application are allowable. Accordingly, the withdrawal of all grounds for rejection and the allowance of all claims are respectfully requested.

**EXCEPT** for issue fees payable under 37 C.F.R. § 1.18, the Director is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. §§ 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-0310. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 C.F.R. § 1.136(a)(3).

Respectfully Submitted,  
**Morgan Lewis & Bockius LLP**

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